

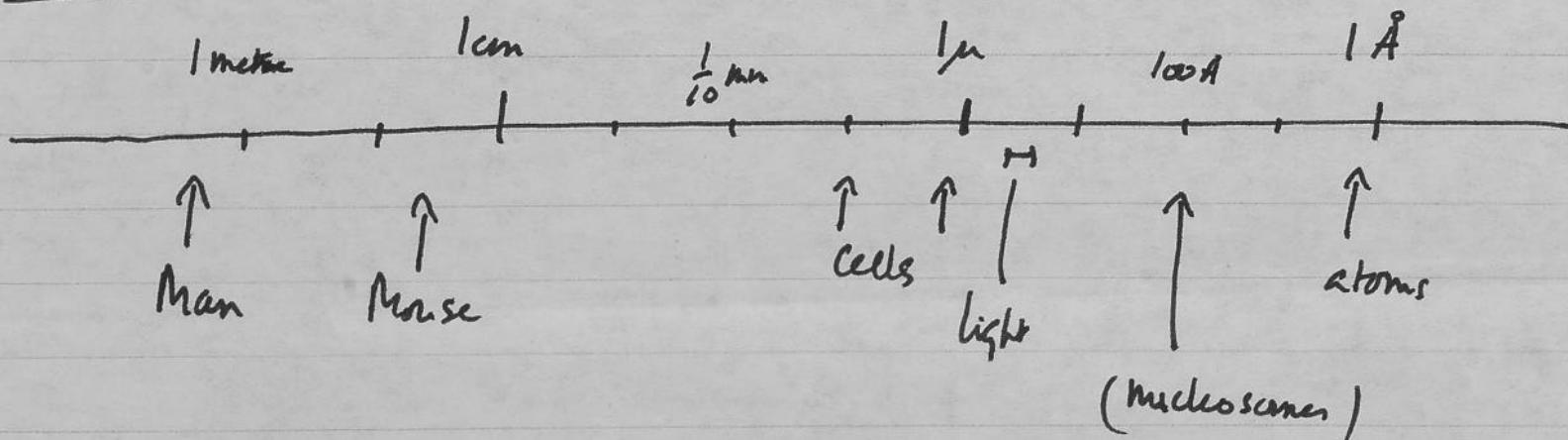
Salk Trustee.

Thursday 20 Jan 1977

## Genes in lower and higher organisms

### Preamble

#### Sizes



What are genes made of nuclear acid?

Ans

Nucleic acid. Two great families. DNA  
(long thin ~~not~~ chain molecules) RNA

Each a backbone + side groups = Bases, 4 types.  
(slightly different)  
Double helix Base-pairing

Life's instructions written in a language with only 4 letters

How big are the instructions?

i.e. how many bases (=bp) in the nuclear acid.

a very small virus SV 40	$\sim 5000$ bp	(1 page)
often E. coli	$3 \times 10^6$ ,	too much
Drosophila	$10^8$	less easily.
man	$3 \times 10^9$	such library
Amphiuma - lunged.	$10^{11}$ bp.	S

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In lower organisms eg bacteria  
(yeast is a 'higher' organism : so is man)

most DNA codes for protein. (20 amino acids  
a gene differentiates  
family of chemicals. triplet  
- machine tools of cell. genetic dictionary)  
(code)

S. u. 40 has ~~just~~ 5-6 (?) genes  
E. coli has ~~not~~  $\approx$  3000 genes.

on this basis man would have  $10^6$  3 million genes.

But genetic estimates only approximate for  $\approx$  50,000  
why this difference? (Same sort of  
problem in morphology, ETC.)

Thus major problem is  
what is all that this DNA for?

① Some must be "junk" ie have a less specific  
function (newspaper or wrapping up fish & chips)

Some Crabs have lots of ATATAT up to 40%.

We ourselves have junk DNA ie single sequence  
but only 10%? (varies in diff organisms)

(2) Some DNA of intermediate complexity

function also unknown.

Is it for regulation?

Complexity of higher organisms:

does this mean more DNA needed for control.

ie more administration ~~attempts~~?

don't yet know.

(3) Much of the DNA is "unique"

but not all codes for protein

ie "Spacer" DNA

also repetition of sequences.

but not in all cases . esp. haemoglobin

Thus this is a major area of our ignorance.

Many approaches

in entire only two  $\frac{A}{B}$ . need to sequence DNA & pure

gene and test its function in the test-tube.

But, measure amounts : need to multiply or up.

- use 'cloning' technique (genetic engineering).  
prior to a "vector" (plasmid) make many copies (danger)

4,

## B Packaging.

total length of DNA per cell  $2 \times 160 \text{ cm}$ .

has to fit in a cell with a nucleus  $\leq 10 \mu$

need to package for cell division ————— S  
DNA multiplies first } picture of  
then chromosomes assort } mitosis.  
then cell divides

Better picture of chromosomes (mouse) ————— S  
(Notice bands).

Contractile ratio (packaging ratio)  $\approx 10^4 : 1$

How is this done.

### Area of Rapid Progress

Special proteins used to help its holding up.

main type called "histones".

4 main types Mw  $\approx 13,000$  ( $\approx 1000$  atoms each + H)

go together (x2) to make a ball about  $10 \text{ nm}$  diameter

DNA wound on outside of ball

Balls are called nucleosome.

(Griffith) SV 40 — S

Fifth type of histone. When added, makes

balls pack together SV 40 — S

to form a filament.

$\approx 100 \text{ \AA}$  diameter.

Balls + their DNA ( $\approx 800 - 140 \text{ bp}$ )

have been crystallized Same Thompson  
Nature

with spacer repeat is  $\approx 200 \text{ bp}$   
 $\approx$  waves.

Contain 2 DNA turns / Ball

Contractile ratio :  $\approx 1:7$  SV 40. — S

Must be more levels of coiling

never been less certain: called a "solenoid" — S

a filament wound round to form a tube thick-walled

tube (prob 5 to 6 balls / turn)

diameter  $\approx 300 \text{ \AA}$  Total contraction ratio  
 $\approx 40$

## New lead

very new, somewhat speculation  
 (Bach + Zentner in Denmark)

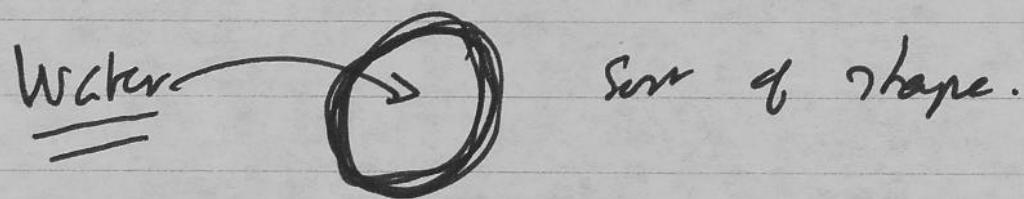
as ~~this~~ open & coil, has this time a

thin-walled tube. 4500 Å (wall 300 Å)

thus can be seen in the high microscope

fairly regular (not double loop) ————— S

the picture, connection, appear to support this



Then last makes a big contract ratio  $\sim \times 40$

$$\therefore 40 \times 40 \sim \underline{1600}.$$

final lead: prob. <sup>the tube</sup> holds (is a collapsed sort of way)

prob. to give another high coil

hence bending in early photo.

perhaps  $\times 5$ .

$$7 \times 6 \times 40 \times 5 \approx \underline{8,000}$$

~~coil~~ which is figure required.

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Thus may now understand packaging for  
mitotic chromosomes. But here are "rest".

Really interesting ones, are transient ones. These  
are or have rarely recorded.

How is perhaps done?

due to special proteins e.g. Histones

but not other proteins help.

Cross-ties??

do some of these persist in transient etc

or in packaging used to control transient  
<sup>help</sup>

to keep some sets of genes rest in  
tissues where they're not needed!

Don't know: how regions are likely to be  
removed. Might have general answer after 5 years.